A NEW FORM OF LOCALIZED LIPOIDOSIS: GRANULOMA CHOLESTERINICUM SUBCUTANEUM[1]

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Within the past few years, the lipoidoses—the diseases of cellular lipoid metabolism—have received increasing attention. Internists, surgeons, dermatologists, physiological chemists, and pathologists employing histologic, histochemical and experimental procedures have been trying to attain a better understanding of the interesting but confusing clinical pictures associated with these diseases. Recently six authors (Thanhauser (1), Montgomery (2), Polano (3), Epstein (4), Sendrail and Basex (5) and Urbach (6)) attempted to classify the entire group of lipoidoses. They failed, however, to reach even partial agreement on the principles of classification. This is probably due to the fact that they set up varying criteria on which to base differentiation; and that none of the criteria selected was sufficiently prominent or important to serve as the one basic distinction. Epstein, for example, establishes his classification strictly from the chemical point of view. Montgomery and Polano combine clinical and chemical considerations, while Thannhauser grants special significance to the pathogenesis (primary essential xanthomatosis vs. secondary xanthomatosis due to hyperlipemia). Urbach bases the subdivision of the different types of lipoidosis on their histologic and chemical nature as well as on the clinical appearance.

However, all these investigators are in complete agreement on one point—namely, that localized and generalized processes must be differentiated from each other. The localized processes were divided by Thannhauser (1) into 2 groups, namely, xanthoma formation in inflammatory processes and those developing in tumors. He included the so-called inflammatory xanthoma of the breast, xanthomatous transformation of the mesentery and xantho-lipomas in the first group. The second group embraces all those tumors having the capacity of lipoid storage within their cells. Such tumors are now generally spoken of as xantheloids in the dermatologic literature.

The group of local processes has been expanded by the addition of recently described lipoid dermatoses featured by degenerative changes. These are the resorption types of xanthelasma (7): necrobiosis lipoidica diabeticorum (8), imbibitio lipoidica telae elasticae degeneratae (9) and imbibitio lipoidica collageni degenerati cutis (6).

We here wish to report on another new form of localized lipoidosis, for which we suggest the designation "granuloma cholesterinicum subcutaneum".

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CASE REPORT

M. B., white male, age 38 yrs., was admitted to the Jewish Hospital, 12/11/40, on the medical service of Dr. Harold Goldburgh. He had had a subtotal gastrectomy in Vienna in 1936, for relief of duodenal ulcer. He felt well for 2 yrs., but in 1938 had pain in the mid-line abdominal incision and was then aware of the presence of several small masses apparently in the depth of the scar. He had them removed in Vienna, but 3 months later they recurred. (We were unable, for obvious reasons, to ask for a report on the histological findings from the Vienna clinic.) Both the original and the secondary operations were performed under general anesthesia. The pain that accompanied the original gastric involvement had not returned but the patient now had almost constant pain, both in the lumbar area and anteriorly under both costal margins. It was not related to eating or any other obvious circumstance. His appetite was good and he tolerated all food except eggs. In spite of this, he had lost 28 pounds in the last 6 months and he was feeling progressively weaker.

Examination revealed a slender, well muscled man in no acute distress. He was afebrile, the pulse was regular and of good volume. There was no superficial adenopathy and the skin was normal. The cardiac action was normal. B.P. was 120/90.

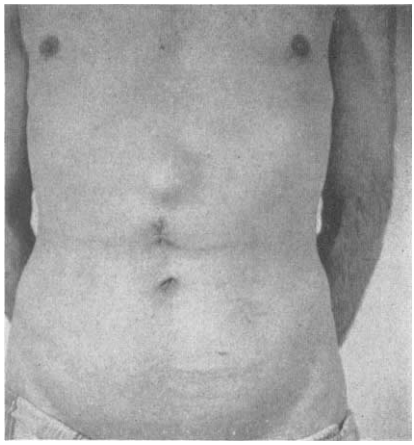

FIG. 1. APPEARANCE OF MASSES IN UPPER MID-LINE OF THE ABDOMEN. FRONTAL VIEW

There was a healed mid-line abdominal scar extending from the umbilicus to the xiphoid process. Midway between these points and beneath the superficial scar there was a well circumscribed round mass, 4 x 4 cms., in diameter (Figs. 1, 2). It was not adherent to the overlying skin and was neither tender nor painful. There were, in addition, several small nodules, also in the mid-line, some 0.75 cm. in diameter, others somewhat larger. They ranged above and below the large mass, along almost the entire length of the incision. They also were not adherent to the overlying skin, which itself appeared entirely normal.

The liver was slightly enlarged and the spleen questionably so. There was definite tenderness in both costo-vertebral angles. Examination of the rectum, prostate, and genitalia revealed nothing of note. The extremities were normal and all reflexes responded normally.

Routine laboratory data were negative except in reference to blood cholesterol. Detailed blood studies, including determinations of the blood sugar, urea, calcium, phosphorus, phosphatase and blood protein fractions revealed normal values. The Van den Bergh and bromsulphalein tests were likewise within normal limits.

Gastroscopy (Dr. H. Tumen) revealed a functioning stoma of a gastro-enterostomy, but no evidence of gastric malignancy or ulceration. X-ray examination of the kidneys and of the spinal column and pelvis revealed no pathologic change.

Biopsy of one of the smaller masses, 12/23/40, revealed it to be a yellow nodular structure, slightly compressible and well attached to the surrounding subcutaneous tissue. Section revealed a soft yellow semi-liquid material, so soft in the center that it escaped leaving an outer wall for histological examination.

On Jan. 13th, 1941, Dr. Ralph Goldsmith excised the large nodule. It was deeply situated, extending in the mid-line to the preperitoneal layer. The mass was very friable and despite great care in its handling, it ruptured and a large amount of yellow homogenous semi-liquid material quite similar in appearance to the yolk of an egg, escaped. Enough reamined, however, for chemical analysis (fat metabolism studies). A section of normal adjacent fatty tissue was also removed for comparative study. The remaining small nodules were dissected out and the wound was closed with silk sutures.

Recovery was uneventful. The patient was discharged 1/18/41. At the time of this report, 1 yr. later, the patient was in good health. There was no recurrence of the nodules, no pain, and the patient gained 30 lbs. He is now eating food without restriction.

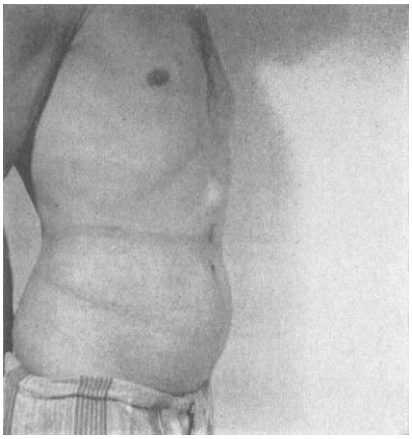

FIG. 2. LATERAL VIEW

HISTOLOGIC FINDINGS

Histologic examination (hematoxylin-eosin stain) of a nodule about 2 cms. in diameter reveals a thick wall enclosing an irregular central cavity. In this wall there are two distinct layers of tissue. There is an outer zone of collagenous fibrous tissue abundantly supplied with dilated arterioles and capillaries. Fairly well circumscribed is an inner zone which on low power magnification is seen to consist of highly cellular tissue (Fig. 3). Its demarcation from the outer fibrous tissue is distinct in many places, brought about by narrow channels, probably lymph spaces. The fibrous tissue immediately adjacent to the inner zone appears to have been under pressure from the inner zone as suggested by the attenuation and compression of the collagen fibrils and adjacent capillaries.

The inner zone is made up of large, pale, vacuolated (foam) cells arranged in solid sheets, which are occasionally broken by small scattered infiltrations of fibroblastic and angioblastic tissue (Fig. 4). The cytoplasm of these foam cells has either entirely disappeared or else is represented by a remaining hazy, pale pink staining debris. The nuclei are small, usually centrally placed, and are

often nucleolated. The cytoplasmic structure is better preserved in the innermost portion of the section, where occasional cells show cytoplasm with a pale,

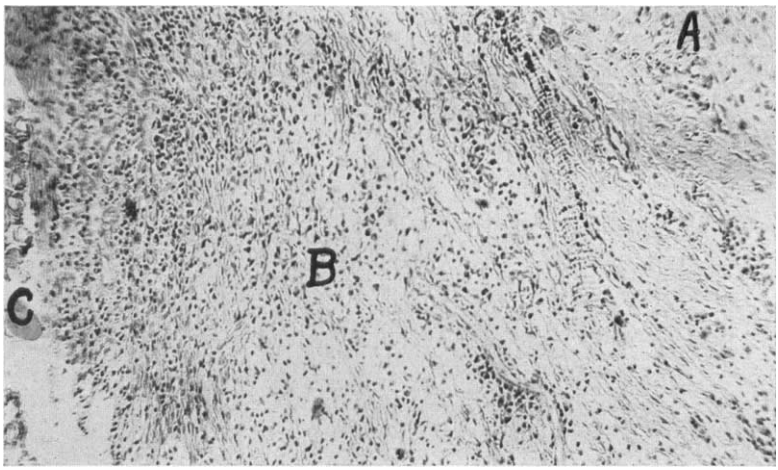

FIG. 3. LOW POWER MAGNIFICATION (100×) OF WALL AND CAVITY OF THE SUBCUTANEOUS NODULE
Outer zone of collagenous tissue (A), inner zone composed chiefly of foam cells (B), cavity containing crystals (C)

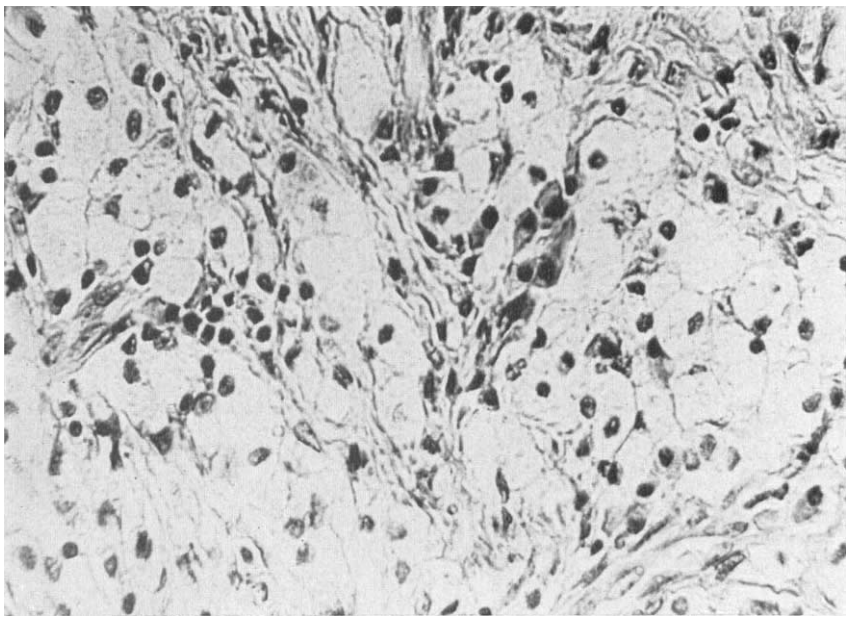

FIG. 4. HIGH POWER MAGNIFICATION (450×) SHOWING "FOAM" CELLS IN THE WALL OF THE SUBCUTANEOUS NODULES

cherry red stain. Small "foam" vacuoles mark the beginning of cytoplasmic destruction.

The innermost portion of this tissue has evidently been compressed, the foam cells in this area being densely crowded. The inner fringe bordering the central cavity is rough without any lining cellular (endothelial) structure, that might suggest that the cavity was a true cyst. Instead it is lined with a wax-like substance taking a dull cherry red stain. Much of this is deposited in irregular

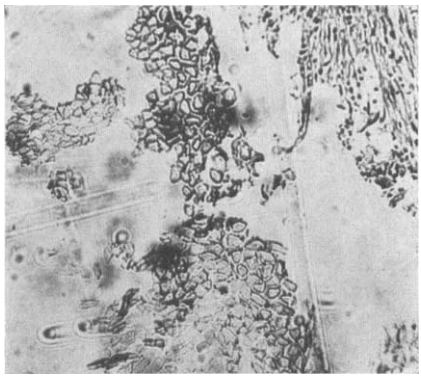

FIG. 5. LOW POWER MAGNIFICATION (100×) OF CRYSTALLINE FORMATIONS WITH ADJACENT CAVITY WALL

(The double contour lines are artefacts)

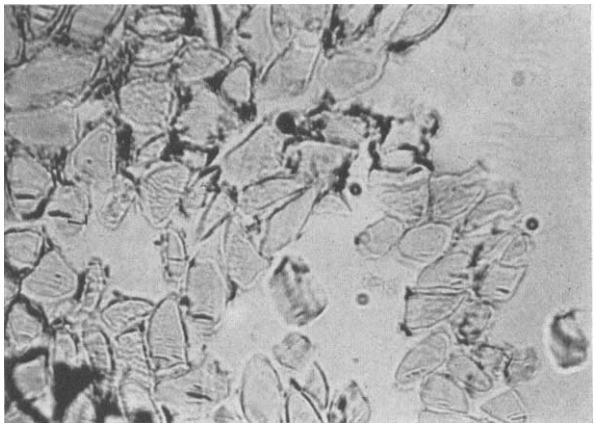

FIG. 6. HIGH POWER MAGNIFICATION (450×) OF THE CRYSTALLINE FORMATIONS IN THE CAVITIES

strands or laminae, crowded and compressed against the enclosing cellular wall. At some points it has been invaded by a few histiocytes. This material apparently is the preserved remainder of an accumulation that formed the central part of the nodule. Some of this substance is lying free within the cavity, but preserving continuity with the portion clinging to the enclosing cellular wall.

There is a striking crystal formation of this material lying within the cavity (Fig. 5). These crystals are translucent, waxlike. Some of them possess a

thick, opaque border taking the cherry red stain mentioned above. The majority have rather sharps edge and are polyhedral (Fig. 6). Others are irregu-

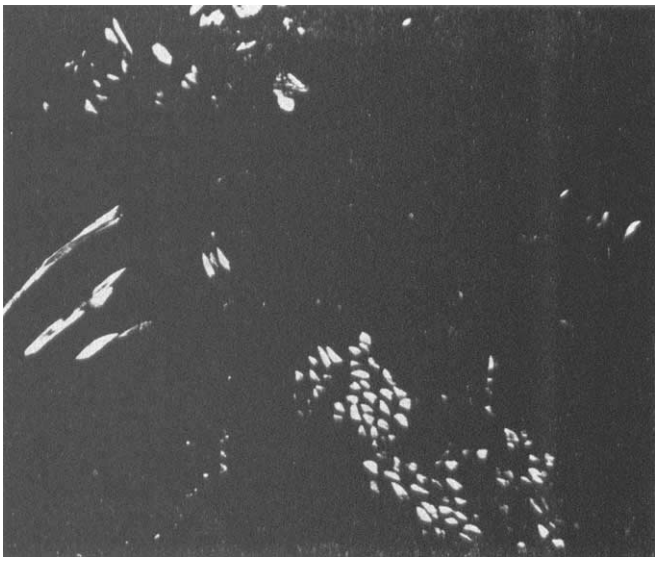

FIG. 7. LOW POWER MAGNIFICATION (100×) OF THE CRYSTALLINE FORMATIONS SHOWING DOUBLE REFRACTIONS (UNDER NICOLL'S PRISM)

Note also the long needle-like wedges as well as the triangular and polyhedral crystals

FIG. 8. HIGH POWER MAGNIFICATION (450×) OF THE CRYSTALLINE FORMATIONS (SEE FIG. 7)

larly faceted by counter pressure. All of them are doubly refractile (Fig. 7, 8) as determined by examination with the Nicol prism and are identified as cholesterol (see histochemical notes).

Section from another nodule reveals essentially the same histologic changes. The lateral portion of the section contains an outer zone of collagenous tissue and an inner zone crowded with foam cells, both zones forming a wall surrounding a ragged central cavity, the contents of which have been lost. The zone containing the foam cells shows, in addition, a large number of infiltrating lymphocytes, plasmacytes, and also fibroblastic tissue, all suggestive of a subacute inflammatory reaction compatible with the definition of granulomatous tissue.

CHEMISTRY

Blood chemistry (Table I) revealed normal values for all fat constituents except cholesterol esters and cholesterol ester fatty acids which were slightly

TABLE I

Fat constituents of blood serum

	MG/100 CC. OF PATIENT'S SERUM	NORMAL VALUES
Total fat	676	570 to 820
Neutral fat	83	100 to 200
Fatty acids		
(a) Total fatty acids	348	190 to 420
(b) Cholesterol ester fatty acids	101	64 to 88
(c) Phospholipid fatty acids	168	115 to 220
(d) Neutral fat fatty acids	79	10 to 170
Cholesterol		
(a) Total cholesterol	240	150 to 200
(b) Ester cholesterol	151	90 to 130
(c) Free cholesterol	89	70 to 90
Phospholipid	252	175 to 330

elevated. The free cholesterol and phospholipids were within normal range. In contrast the tumor tissue showed a striking increase of cholesterol and phospholipids as compared to the fat tissue of a normal subject. Thus the toal cholesterol (Table III) is more than 27 times the value of fat tissue in normal individuals as determined by Eckstein and Wile (10), Urbach, Epstein and Lorenz (11), the cholesterol ester 34 times, the free cholesterol 160 times and the phospholipids 323 times. As can be seen from this table, there are also considerable differences between the fat tissue adjacent to the tumor and the normal subcutaneous fat tissue.

These findings closely correspond with those which Eckstein and Wile (10) have reported in a large pedunculated xanthomatous tumor from the buttock and from the surrounding subcutaneous fat which appeared grossly normal (Table III). In their case, too, the adjacent fat contained 12 times as much phospholipids and four times as much cholesterol as normal fat. Whether this

increase is actually due to the underlying metabolic disorder or merely represents an infiltration from the xanthomatous tumor, the authors were unable to

TABLE II

Fat constituents of the tissue

	TUMOR (GM./100 GM. DRY WEIGHT)	ADJACENT FAT TISSUE (GM./100 GM. DRY WEIGHT)	NORMAL SUBCUTANEOUS FAT (GM./100 GM. DRY WEIGHT)
Total fat	90.1	95.7	95.8
Neutral fat	40.3	94.3	
Fatty acids			
(a) Total fatty acids	46.0	90.3	95.95
(b) Cholesterol ester fatty acids	2.9	0.3	
(c) Phospholipid fatty acids	0.8	0.3	
(d) Neutral fat fatty acids	42.3	89.7	
Cholesterol			
(a) Total cholesterol	5.55	0.65	0.204
(b) Ester cholesterol	4.3	0.45	0.125
(c) Free cholesterol	1.25	0.20	0.079
Phospholipids	1.29	0.50	0.04

TABLE III

Comparison of xanthomatous tissue, adjacent fat tissue and normal fat tissue

Grams per 100 grams dry weight

	REFERENCE	TOTAL CHOLESTEROL	FREE CHOLESTEROL	CHOLESTEROL ESTERS	FREE CHOLEST:CHOLESTEROL ESTERS	PHOSPHOLIPIDS	FATTY ACIDS
Subcutaneous tumor	Present case	5.55	1.29	4.30	1:3	1.29	46.0
Adjacent fat tissue	Present case	0.65	0.20	0.45	1:4.4	0.50	90.3
Xanthomatous tumor	Eckstein & Wile (10)	8.59				1.42	
Adjacent fat tissue	Eckstein & Wile (10)	0.34				0.16	
Extracellular cholesterosis	Urbach, Epstein & Lorenz (11)	3.31	2.51	0.8	3:1	1.18	6.9
Adjacent fat tissue	Urbach, Epstein & Lorenz (11)	0.26	0.157	0.104	1.5:1	0	94.19
Normal subc. fat tissue	Urbach, Epstein and Lorenz (11)	0.204	0.079	0.125	1:1.6	0	95.95
Normal subc. fat tissue	Eckstein & Wile (10)	0.24				0.04	

decide. Table III includes the only two previous reports on the lipoid chemistry of xanthomatous tumors. All the other determinations on xanthelasmas recorded in the literature do not contain figures on the surrounding fat tissue.

Since the present discussion is concerned with a lipoid tumor situated in subcutaneous tissue exclusively only those chemical analyses are pertinent in which subcutaneous tissue was also studied.

The ratio free cholesterol/cholesterol ester in our case is 1:3. This is important because this ratio is exactly the opposite in extracellular cholesterosis (11) (3:1). On this ground alone, the present case has to be segregated from the lipoid disorder.

DIFFERENTIAL DIAGNOSIS

Is the lipoid disease under consideration a xanthelasma situated in the subcutis? (We (13) prefer the term "xanthelasma" to "xanthoma" because a blastomatous character, as suggested by the suffix "oma," is demonstrable only in extremely rare cases.) So far as we know localized xanthelasmas in the subcutis have been described only twice in the entire literature: once by Corten (14) (in a man), and once by Nitsche (15) (in a horse). It seems most unlikely, however, that Corten's case was a xanthelasma, for the author himself assumed on histological grounds, that the condition had arisen as the result of a misplaced anlage of a sebaceous gland. Nitsche's case appears to be one of lipophage granuloma (see below) which developed subsequent to trauma. The chief reason, however, that xanthelasma should be excluded from consideration is the fact that the presented case shows histological and chemical features never recorded in xanthelasma. These are massive deposits of cholesterol filling cyst-like cavities. For the same reasons the diagnosis of xantheloids (xanthofibroma, xantholipoma, etc.) can be ruled out.

Because the nodules in this case developed subsequent to an operation and invariably in the vicinity of the site of the operation, consideration must be given in some detail to the so-called "resorption-type" of xanthelasma. We understand this term to designate a deposition of cholesterol esters and of free cholesterol in scars or in otherwise injured cutaneous areas, in association with normal cholesterol metabolism (13). We are not as yet in a position to know whether in such cases, the lipoid substances are liberated by the pathologic process in the tissue or whether they are derived from the blood. These conditions include primarily the "scar xanthomas" (Weidmann (16))—as, for example, in scars in tertiary syphilis (Urbach, Truffi), in lupus scars (Brauer), in laparotomy scars (Posner, Weidmann and Stokes), in vaccination scars (Knowles and Fischer), in herpes zoster scars (Weidmann, Kreibich), in the atrophic skin in dermatitis atrophicans (Ehrmann, Jessner). Also to be included here are processes encountered not infrequently in internal organs, in which local inflammation brings about absorption of cholesterol ester by altered cells, which then show "foam" structure. Processes such as pyosalpinx and chronic cholecystitis frequently exhibit such histological and chemical alterations. Considered as a group they have been termed "degenerative inflammatory cholesterosis" by Aschoff and Siemens. Earlier writers employed the designation "pseudo-xanthomas" or "xanthomatous degeneration." The modern terminology prefers (13) the term "resorption xanthelasma." A local tendency to cellular

absorption of cholesterol must be assumed, because tissue damage does not per se lead to the development of local xanthelasma even in individuals with hypercholesterolaemia or even with xanthelasma already present in other parts of the body. Thus Weidman (17) attempted to reproduce xanthelasmatous scars experimentally in 10 hypercholesterolemic volunteers. Examination of the excised skin showed no xanthelasmatous lesions. Schmidt (18) allowed silk threads to remain for 3 months in the skin of a patient with generalized xanthelasma. No local manifestations were thereby elicited.

In all reported cases of "xanthomatous scars" the xanthelasma formation was observed in the scars themselves or in the adjacent skin areas. In our case, on the other hand, the skin above the tumors remained entirely free from xanthelasmatic deposits; the lipoid nodules were located exclusively in the subcutaneous tissue, and formation was extreme; we feel, therefore, that our case should not be included in the group of "resorption-type" of xanthelasma.

We must next consider the group of lipophage granuloma or lipogranuloma. This group includes various fat containing tumors, which have hitherto been within the province of the surgeon and of the pathologist rather than of the dermatologist.

The surgeons of half a century ago were well acquainted with granuloma formation seen in association with focal necroses of the subcutaneous fatty tissue. At that time, of course, they were unable to perform special fat strains or chemical lipoid determinations. It is possible, of course, that some of these lesions were identical with that herein described. Designations such as "traumatic fat necrosis" (Lanz), "traumatic cysts" (Sasse), "subcutaneous fat necrosis" (Berner, Hyde) "subcutaneous fat cleavage" (Küttner), "oleo-granuloma" (Henschen) are revealing. Lee and Adair (19) were the first to engage in a systematic study of this type of tumor which appears most commonly in the breast, but sometimes also in the subcutaneous tissue between the skin and the mammary gland and which can reach a size of 7.0 cm. in diameter. The chief importance of these lesions—called "traumatic fat necrosis" by Lee and Adair—is that they are almost always mistaken for carcinoma of the breast. The work of Stulz and Fontaine (20) should be specially referred to since these authors introduced the term "lipophage granuloma" to replace "traumatic fat necrosis."

The attention of Abrikosoff (21) and other Russian pathologists was attracted to the lipophage granulomas during the typhus epidemic in Russia in the years 1920–21. After extensive investigation, Abrikosoff concluded that focal necrosis of the fat tissue can develop under the influence of a number of toxic and infectious conditions or circulatory disturbances, as the result of changes in the blood vessels or of vasomotor disturbances. Clinically, they manifest themselves in the form of small nodules in the subcutaneous fat tissue. The pathologic-anatomic explanation has been, that following toxic or infectious damage, the liberated saponified fat may act as a foreign body in the tissue. In this capacity the fat elicits local reactive processes consisting of the appearance of giant cells of the type of foreign body giant cells, which in turn absorb the fat. In a more advanced stage the fat granulomas sometimes change into cyst-

like cavities, which are at first filled with fat; their walls consist of "granulation" as well as of connective tissue.

Abrikosoff divides the lipophage granulomas into four etiologic types: (1) the artificially induced, or injection, granulomas, which developed following infection of fatty substances, usually camphorated oil; (2) the traumatic granulomas, resulting from traumatic destruction of the fat tissue; (3) granulomas which develop in the vicinity of inflammatory processes; (4) spontaneous lipophage granulomas, due to spontaneous focal necrosis of the fat tissue, apparently of ischemic origin.

Similar nodule- and cyst-formations have been described in detail by Makai (22). He chose to term the condition "lipogranulomatosis subcutanea."

Bartsch (23) described three cases which presented firm nodules in the subcutaneous fat tissue. When bisected these nodules were found to be hollow, filled with an oily substance; their walls were firm. Microscopic examination revealed granulation tissue rich in cells and collagenous fibers, lymphocytes, polyblasts, leucocytes, fat-phagocytes, foam cells, polynuclear giant cells, along with ray-formation and druse-like deposits of the calcium salts of soap.

Finally, the so-called cholesteatoma should also be mentioned here. Johannes Müller, who introduced the designation "cholesteatoma" many decades ago, intended to describe nothing more than epithelial formations containing cholesterin crystals. Subsequently, however, this term was also employed to designate tumor-like formations. Thus Dorland (24) defined cholesteatoma as: (1) a tumor of a crystalline structure, occurring mainly in the brain; (2) a tumor of the middle ear, the mucous membrane of which assumes a skin-like character, becomes inflamed and degenerated.

The results, however, of more recent investigations seem to indicate that cholesteatoma is now to be considered in a different light. Thus Kaufman (15) states: "The so-called cholesteatomas of the ventricle plexus in humans, which may reach the size of beans and are of yellow-white, rounded, tumor-like inclusion similar to the larger tumors of horses (Joest, Saul) are not true cholesteatomas, but infectious granulomata with embedding of doubly refracting substances in the cells (the so-called pseudoxanthoma cells) and of cholesterin needles, about which are grouped foreign body giant cells." According to Saul (26), the cerebral plexus cholesteatoma in horses is attributable to blood thrombi of the plexus tissue which develop as the result of local streptococcus infection, and which have a high cholesterol crystal content, because of the normally high cholesterol content of horse's blood. After organization of the thrombus there develops a granuloma, high in cholesterin content, called "granuloma cholesterinicum" by Schmey (27). This entire sequence suggests that the cholesteatoma of the cerebral plexus might perhaps more logically be included among the lipophage granulomas.

Nor are the cholesteatomas in the middle ear and external auditory canal, according to French otologists (Lemaitre and Lavrand (28), Mounier-Kuhn 29)) cholesteatomas in Müller's sense; for, from their histologic structure, they would seem more properly regarded as "histiocytomes xanthélasmisés." On the bases

of these newer histologic findings, it would seem desirable to avoid the older and indefinite interpretation of the term "cholesteatoma." This is also the opinion of one of the outstanding authorities of lipoid diseases, Weidman (30), when he writes in a critical analysis of cholesteatoma: "The scope of the term 'cholesteatoma' is thus broad enough to include cutaneous xanthoma as cholesteatoma."

It cannot be denied that, both clinically and chemically, our case bears a certain resemblance to the so-called cholesteatomas of the ventricle plexus; on the other hand, there are some profound histologic and probably pathogenetic differences. Thus Saul (26) is of the opinion that the cerebral plexus cholesteatoma in horses is caused by deposition in blood thrombi of cholesterol from the blood.

The other local lipoidoses mentioned above need not be considered here, since they bear no clinical, histologic or chemical similarity to the disease-entity here described.

On the basis of these differential-diagnostic considerations, it is believed that granuloma cholesterinicum subcutaneum is not to be identified with any of the local or generalized lipoid diseases that have hitherto been reported.

COMMENT

In view of the slightly increased cholesterol value in the blood serum (240 mg. %), is it justifiable to regard the dermatosis under consideration as a local lipoidosis? In answer to this question we take the same stand as we took with regard to the classification of necrobiosis lipoidica diabeticorum and the imbibitio lipoidica collageni degeneratae cutis which are always accompanied by hypercholesterolemia: we consider a condition to be a local lipoidosis when it is caused by a primary local disease of the tissue (trauma, infection, intoxication) with a secondary deposition of lipoid in the involved tissue. In the case herein described the blood cholesterin level was only slightly elevated and we would rather consider it as high normal.

The outstanding and essential characteristic of the local tumors described is their enormous cholesterol content, which is 27 times that of the subcutaneous fat tissue in normal human beings and $8\frac{1}{2}$ times that of the fat tissue adjacent to the tumor. Furthermore, they display another characteristic which as far as could be found in the literature has never before been described—namely, the aggregations of cholesterol crystals. Aside from the cases reported by Bartsch (23), in which there was a druse-like formation which he interpreted as calcium soap deposits (unfortunately more intensive histochemical and chemical examinations were not undertaken), there is only one other lipoid disease (generalized) in which somewhat similar findings have been made: the Bogaert-Scherer syndrome (12). These Belgian authors have described a disease which is characterized by vast depositions of cholesterol in crystal form in the brain and in the tendons. This disease is characterized on the one hand by central nervous system symptoms in the form of progressively increasing disturbances in the cerebral nerves and in the innervation of the lower extremities, and, on the other hand, by the development of "cholesterol gout" nodules in the tendons. Chemi-

cally Epstein (31) has demonstrated a reversal of the normal cholesterol ratio in these tumors: that is to say proportion of free cholesterol to cholesterol ester has shifted to the advantage of free cholesterol—a change similar to the one demonstrated by Urbach, Epstein and Lorenz (11) in extracellular cholesterosis. The present case, however, differs from the Bogaert-Scherer syndrome in that it is strictly localized in the subcutaneous fat tissue.

We are unable to explain the pathogenesis of this case. While it is true that the tumors appeared approximately two years after an operation and were confined to the vicinity of the operative site, the writers prefer to consider this trauma as the trigger-mechanism, rather than the fundamental cause. For, despite countless operations involving traumatic damage to the abdominal fat tissue, no such case has been reported in the entire surgical and pathological literature.

Morphologically this lipoid dermatosis is to be included in the group of localized lipoid granulomas. This term was coined by Chester (32) to point out that the xanthelasmas are non-bacterial, chemically induced, chronic granulomas. When the lesions are spread over the entire body he employs the term "lipoid granulomatosis." The lipoid granuloma is characterized by three types of cells: typical foam cells, exudate cells and young connective tissue cells. While all these cells were found in our case, the lipoid was principally composed of cholesterol ester and free cholesterol. Hence it is felt that the general designation of "lipoid granuloma" should here be replaced by the more specific "granuloma cholesterinicum subcutaneum."

SUMMARY

1. Cutaneous lipoidoses can be divided on clinical and pathogenetic grounds into generalized and localized types.

2. The localized group is composed of (a) resorption type of xanthelasma, (b) necrobiosis lipoidica diabeticorum, (c) imbibitio lipoidica tela elasticae degeneratae cutis, (d) imbibitio lipoidica collageni degenerati cutis.

3. A new entity of localized lipoidosis is presented—"*granuloma cholesterinicum subcutaneum.*" The distinguishing and characteristic features are: massive extracellular crystalline deposits of cholesterol esters and free cholesterol in cyst-like cavities. They are surrounded by granulomatous tissue of conspicuously lipoid character. These formations are situated solely in the subcutis without any involvement of the overlying skin.

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DISCUSSION

DR. FRED WEIDMAN, *Philadelphia:* The part of the paper that I listened to particularly closely was in respect to the differential diagnosis from lipophagic granuloma, and it was not quite clear to me on what basis that the latter diagnosis was excluded. Obviously, I have not been able to study this case as attentively as Dr. Urbach has, but it seemed to me that this lesion might possibly be of the order of traumatic fatty cysts, followed by lipophagic granuloma. Dr. Urbach indicated that he had considered the fact that the lesions occurred in the neighborhood of scarring, and that a time period of two years had elapsed between the operation and recognition, at least, of the cyst, but unless there is something more definite forthcoming in the way of some other pathogenic mechanism, I think that a traumatic factor would be the logical thought which would first occur to mind. I will grant the rather difficult item to explain in the form of that period of two years which elapsed before the appearance and development of the fatty masses.

In respect to the partition of lipoids in the cystic masses, in which cholesterol is stressed, that is entirely different from the lipoid partition such as occurs in living tissues like the blood in xanthoma. For example, I understand that the lesions in Dr. Urbach's case were cystic; that means that these masses were beyond the control of body metabolic processes. To all intents and purposes, these accumulations were decomposing. From them there will be absorption of fats from time to time, and from month to month the lipoid partition in the cystic masses can and must change. Accordingly, it is not at all surprising that on different occasions there would be differing proportions of lipoids, particularly of cholesterol; the earlier the lesion, the smaller the amount of cholesterol, whereas at a later stage it would be greater because the neutral fats can become saponified and thereafter absorbed.

In short, I do not believe that these lesions rate as a separate clinical entity. The considerations in respect to the lipoids in them revolve around the irregular changes that occur in decomposing fatty accumulations in general and have little, if any, relationship to general fatty metabolic processes, and in which cholesterol and fatty acids regularly accumulate as time goes on. The story is the one of secondary retrogressive changes in fatty masses at large, and which is told conventionally in general pathologic states.

LOUIS A. BRUNSTING, *Rochester, Minnesota:* Inasmuch as this lesion developed adjacent to the site of an operative scar, I am wondering about its being the expression of a foreign body reaction, perhaps due to the accidental implantation of talcum powder in the wound. There were some interesting examples of this type of reaction portrayed in the dermatologic division of the Section on Scientific Exhibits of the American Medical Association at the current meeting.

DR. DONALD PILLSBURY, *Philadelphia:* On many occasions I have had the opportunity to observe work which Dr. Urbach has reported upon since he became associated with the University of Pennsylvania, and there is no question but that many of these patients show a difference from the lipoid diseases with which we are familiar. There is one general point which I would like to emphasis: We realize that there is no satisfactory classification for lipid diseases, and the terminology associated with these has become extremely complex.

In discussing this problem with others, and attempting to interpret some of the importance of dermatology I got the strong feeling that much of the difficulty is due to the fact that we do not talk the same language. I would therefore urge that in this instance, as regards lipoidosis, the terminology not be made more complex if it can be avoided. I think this should hold true throughout dermatology, and we who have a better appreciation of our aims, should bear this in mind.

DR. ERICH URBACH, *Philadelphia:* I believe Dr. Pillsbury is absolutely right when he states that dermatologists in various countries employ different nomenclatures. I have mentioned that men in four different countries have attempted in the last few years to arrive at a common classification of lipoidosis, and they could not agree because they speak different scientific languages. They consider different things important, although it is necessary to find a common basis. One common ground would be to distinguish lipoidosis in its generalized and localized forms. I have demonstrated here the localized lipoidosis in other words, localized disturbance. This means that first there was injury to the tissue and secondarily the lipid disturbance developed.

I wish to thank Dr. Weidman for his discussion. I can appreciate his criticism concerning the possibility of lipoid granuloma, since he did not see the slides in this case. I have been familiar with the lipoid granuloma for a long time, but when I saw the chemical investigations, which showed that these cysts contained chiefly free cholesterol, cholesterol esters and phospholipids, and when I compared this to the findings in normal tissue, it became evident that this case was not lipoid granuloma but a localized lipoidosis, characterized by a tremendous amount of cholesterol. I therefore took the liberty of distinguishing this particular condition, and designating it by a more specific term.